Interrupting the transmission of wild polioviruses with vaccines: immunological considerations

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In 1988 the World Health Assembly set the goal of global poliomyelitis eradication by the year 2000. Substantial progress has been made, and 143 countries reported no poliomyelitis cases associated with the wild virus in 1993.

This article reviews the immunological considerations relevant to interrupting the transmission of wild polioviruses with vaccines. Although serum immunity prevents poliomyelitis in the individual, it is local immunity that is important in preventing the transmission of polioviruses in the community. Natural infection and vaccination with oral polioviruses vaccine (OPV) produce local immunity in the intestine and the nasopharynx in about 70–80% of individuals. In contrast, inactivated poliovirus vaccine (IPV) produces local intestinal immunity in only 20–30% of the individuals. With either vaccine, however, a substantial proportion of the immunized population can transmit the wild virus. Moreover, although serum immunity is long-lasting, limited data suggest that local immunity may not be as persistent.

To interrupt the transmission of wild polioviruses efforts should be made to achieve and sustain high levels of poliovirus vaccine coverage. Recent outbreaks show that wild poliovirus poses a risk for unimmunized individuals, even when overall coverage levels are high. Delivery of poliovirus vaccine to hard-to-reach populations will be of increasing importance as countries progress toward the final stages of poliomyelitis eradication. The immunization status of persons from poliomyelitis-free countries should be updated prior to travel to poliomyelitis-endemic areas.

Introduction

In May 1988, the 41st World Health Assembly established the goal of global eradication of poliomyelitis by the year 2000. Specific targets include both the elimination of paralytic disease caused by wild poliovirus and the elimination of the wild virus itself.

Progress has been rapid in eliminating disease due to wild poliovirus. In 1993, a total of 143 countries/territories reported to WHO no cases of poliomyelitis associated with the wild virus. Areas that are free of poliomyelitis now include North America, South America, Japan, and Australia. In addition, disease-free zones appear to be emerging in southern Africa, North Africa, Europe, the Middle East, and the Western Pacific.

The eradication of poliomyelitis is often compared with that of smallpox. However, in contrast to infection with variola virus, most persons infected with poliovirus remain asymptomatic and can excrete the virus for several months. Outbreaks of poliomyelitis in Finland (*2*), the Netherlands (*3, 4*), and Oman (*5*) suggest that wild polioviruses can replicate in well-immunized persons who have no clinical disease, spread to other persons, and eventually induce paralytic poliomyelitis in susceptible individuals.

This review examines the immunological considerations relevant to interrupting the asymptomatic transmission of wild polioviruses with vaccines. Summarized are published studies from two eras. First, to review the mechanisms of spread of poliovirus and the immune response of individuals to infection with wild and vaccine viruses, particular attention has been paid to studies conducted in the 1950s and 1960s. Second, to gain insight into recent transmission patterns of polioviruses, selected lessons from recent poliomyelitis outbreaks are reviewed.

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Mechanisms of person-to-person spread of polioviruses

By the mid 1960s, the pathology of poliomyelitis had been well described (*6*). The course of poliovirus infection can be divided into the following steps: implantation and replication of the virus at the primary portals of entry (the oropharyngeal mucosa and the intestinal mucosa); spread of the virus to the tonsils and deep cervical nodes in the oropharyngeal region and to Peyer's patches and the mesenteric lymph nodes in the lower alimentary tract; entry of the virus into the bloodstream, resulting in viraemia; and establishment of infection in the central nervous system.

Poliovirus can implant and replicate independently in the throat or the intestine (*7*). Virus is shed from the nasopharynx for up to 3–4 weeks after infection and can be isolated from the throat for about a week, with peak levels of 10^5–10^6 $TCID_{50}$ per swab (*8*). Large amounts of virus are shed in the faeces for up to 5–6 weeks (*9*). Once excreted, poliovirus can survive outside the human body for weeks at room temperature and for many years at –20 °C (*10*).

There are two routes of spread of poliovirus—faecal–oral and nasopharyngeal—and their importance varies, depending on the level of sanitation and the population density. Where sewerage systems are well developed and water remains uncontaminated, the faecal–oral mode of spreading will be reduced. For countries where the level of sanitation is high, the main route of poliovirus infection is droplets or aerosol from the nasopharynx; whereas, for countries with a low level of sanitation, infection is mainly by the faecal–oral route (*11*). However, to some extent this classification is artificial, since in all countries infant stools are an important source of faecal–oral spread and in all countries coughing and sneezing can spread polioviruses.

Immunity and the role of different classes of antibodies

Natural infection with poliovirus initiates a complex process that eventually results in both humoral and mucosal immunity. Both humoral and mucosal immunity are important in protecting the individual against paralytic poliomyelitis.

Humoral immunity

The two components of humoral immunity are cell-mediated immunity and antibody-mediated immunity. Cell-mediated immunity to polioviruses has been insufficiently investigated in humans (*12, 13*), whereas antibody-mediated immunity has been well studied. IgM and IgG antibody are detected in the serum as early as 1–3 days following natural infection (*14*). The level of serum IgM antibody is higher initially, but disappears after 2–3 months. The IgG level increases over the same period and is the predominant long-lasting serum antibody (*15*). Serum IgA antibody is detected approximately 2–6 weeks following exposure, but remains at a low level rising only slowly during the first 3 months after exposure (*14*).

Mucosal immunity

Replication of poliovirus in the epithelium of the pharyngeal and intestinal mucosa produces local antibody and mucosal immunity to poliovirus. The predominant class of immunoglobulin in alimentary tract secretions is IgA, which possesses neutralizing activity against poliovirus (*14*). Secretory IgA antibody can protect against infection of the alimentary tract with polioviruses, but the resulting local immunity is not absolute and a sufficiently large dose of poliovirus can replicate in the oropharynx and the intestine even in the presence of secretory IgA (*16, 17*).

Protecting the individual and the community

Individual protection against paralytic poliomyelitis is provided by IgG antibody, which neutralizes polioviruses in the serum, preventing them from reaching the central nervous system. Although this is a very effective protective mechanism, individuals who lack serum IgG may be resistant to reinfection with polioviruses if their level of secretory antibody is sufficiently high (*14, 18*).

Blocking person-to-person transmission of poliovirus depends primarily on the presence of local secretory antibody in the pharynx and the intestine, which restricts poliovirus replication (*16*). The ability of mucosal immunity to block the replication and shedding of polioviruses may be amplified by a high level of serum IgG antibody, although the primary defence barrier appears to be local secretory IgA antibody.

Immunity after natural infection and after vaccination

Serum antibody response

The serum antibody response (for IgM, IgG, and IgA) is similar following natural infection, immunization with oral poliovirus vaccine (OPV) or with inactivated poliovirus vaccine (IPV), although IgG

antibody levels following natural infection are two to four times higher than those observed following immunization (*14*).

In industrialized countries, numerous epidemiological and clinical studies have demonstrated similar high levels of IgG antibody following immunization with either OPV or IPV (*14*). However, in developing countries, the response to OPV is quite varied, and the studies conducted in developing countries over the past 25 years have reported a wide range of seroconversion rates after three doses of OPV: 73% (range, 36–99%) for type 1; 90% (range, 71–100%) for type 2; and 70% (range, 40–100%) for type 3 (*19*). In developing countries the neutralizing antibody response to two doses of IPV (the first dose given at ≥8 weeks of age with an interval of ≥1 month between doses) is ≥87% for type 2 and type 3 poliovirus, and ≥94% for type 1.[a]

Local immune response in the intestine

Natural infection with wild poliovirus induces local immunity, and secretory IgA antibody develops in the intestine approximately 2 weeks after infection (*14*). Administration of OPV also induces local intestinal immunity (*14, 20*). In contrast, IPV is not very effective in inducing local immunity in the intestine (*14*), and following vaccination with IPV, the intestinal tract of most persons remains susceptible to reinfection with polioviruses (*20, 21*).

Most investigators have found that the degree of intestinal immunity after natural infection or vaccination with OPV varies with the serotype of poliovirus and that local immunity is lower following type 3 infection than that following infection with type 1 or type 2 poliovirus (*22, 23*). In contrast, Benyesh-Melnick et al. (*24*) found that children with antibodies caused by natural infection with poliovirus were immune to reinfection with all three serotypes to the same extent.

The local immune response in the intestine varies depending on whether it is induced naturally or by vaccine. A study conducted in 1960 in the USSR provides quantitative comparisons of these differences (*20*). This study used an oral challenge dose of 10^6 $TCID_{50}$ of attenuated type 1 poliovirus and monitored faecal excretion of the challenge virus for 30 days. Individuals with permanent paralysis due to poliovirus demonstrated absolute mucosal immunity: none of them shed the poliovirus following challenge. Among children who were naturally immune (but without paralysis), only 34% shed challenge virus, compared with 80% of children who were not immune. Mean virus excretion was 5.1 days for the naturally immune children, compared with 20.4 days for the nonimmune children. The mean virus titre per gram of stool was 1000 times higher among the nonimmune children. Among children previously immunized with three doses of OPV, 37% excreted challenge virus, but the time of excretion was short (mean, 4.6 days) and the virus titre per gram of stool was low. Among children immunized with two doses of IPV (all of whom developed serum antibody titres of ≥1:128), 74% excreted the challenge virus. The period of virus excretion was three times longer among IPV-vaccinees than among OPV-vaccinees and the quantity of virus per gram of stool was 100 times higher among IPV-vaccinees.

In 1991, Onorato et al. published a similar challenge study (*17*). Following oral challenge with 10^6 $TCID_{50}$ of attenuated type 1 poliovirus, 31% of children who had received three doses of OPV shed the challenge virus in stools, whereas virus was shed by 82% of children who had received three doses of enhanced-potency IPV (eIPV). As in the earlier USSR study, the eIPV-immunized children excreted challenge virus for longer (mean, 15.5 days) than OPV-immunized children (mean, 6.4 days). At 42-days post-challenge, 9% of the eIPV vaccinees were still shedding the virus.

In addition, Onorato et al. measured directly the level of secretory IgA in stools, and found that a similar proportion of children vaccinated with three doses of OPV or three doses of eIPV had secretory IgA antibody in stool specimens (*17*). However, while a high level of secretory IgA restricted excretion of attenuated type 1 poliovirus in the stools of OPV-vaccinees, this did not occur with eIPV-vaccinees. For the eIPV-vaccinees, poliovirus-specific IgA levels in their stools did not correlate with poliovirus excretion. These data suggest that secretory IgA antibodies induced by OPV may be qualitatively superior to secretory IgA antibodies induced by eIPV.

Local immune response in the pharynx

Although IPV is not very effective in decreasing shedding of poliovirus from the intestine, it is more effective in reducing poliovirus shedding from the pharynx. Studies by Wehrle et al. showed that, following contact with patients who had paralytic poliomyelitis, poliovirus occurred less frequently and at a lower titre in the pharynx of IPV-immunized persons than unimmunized persons (*25*).

When eIPV became available in 1978, it was suggested that this more potent vaccine might stimulate a greater secretory antibody response in the

[a] **Robertson SE.** Poliomyelitis. In: *The immunological basis for immunization.* Unpublished document WHO/EPI/93.16, 1993.

nasopharynx. However, Zhaori et al. found that secretory IgA neutralizing antibody in the nasopharynx was more effectively induced by OPV (70% of vaccinees) than by eIPV (27% of vaccinees) (*26*). Similar data were obtained by Faden et al. (*27*).

Zhaori et al. showed that the secretory IgA antibody induced by eIPV in the nasopharynx has less specific antibody activity than that induced by OPV (*28*). Possibly the weak mucosal immunity obtained with eIPV may be due to the different antigenic site-specificity of IPV-induced antibodies, compared with antibodies produced after infection with wild or attenuated poliovirus.

Relationship of serum antibody and secretory immunity

Studies on the relationship of serum antibody levels to the degree of local immunity are equivocal. Several investigations have found that suppression of poliovirus replication in IPV-vaccinees was largely dependent on the levels of pre-existing serum antibodies (*25, 29, 30*). For example, Glezen et al. reported that low titres of pre-existing serum antibody were associated with a decrease in excretion of attenuated poliovirus from the oropharynx, but that higher titres of serum antibody (≥1:128) were required to decrease excretion in faeces (*30*). On the other hand, Verlinde & Wilterdink showed that faecal excretion of attenuated poliovirus occurred in naturally immune individuals, irrespective of whether they had high or low titres of serum antibody (*31*). Similar findings were reported by Onorato et al. (*17*). The discrepancy between these findings may be because of the presence of previous, inapparent poliovirus infection in some of the children studied.

Long-term serum and secretory immunity

Duration of serum antibody

After natural infection with poliovirus, serum IgG antibody persists for many years. For example, in an isolated Eskimo population, IgG antibody persisted for at least 40 years after natural infection in the absence of any further exposure to poliovirus (*15*).

Reports of the persistence of antibody after vaccination with OPV have varied. One serological survey carried out 15 years after national OPV campaigns found virtually 100% antibody prevalence among persons aged ≥2 years (*32*). In a prospective study where vaccinees were followed for 5 years after primary immunization, serum antibodies to type 1 poliovirus were found among 92–98%, to type 2 among 98%, and to type 3 among 84–87% (*33*). Other studies report a decline in OPV-induced neutralizing antibodies with time (*34*). However, data on the persistence of neutralizing antibodies among persons living in areas where OPV is also used for mass vaccination should be viewed with caution since antibody titres can be boosted as a result of the community spread of OPV viruses (*33*).

The duration of serum neutralizing antibody after IPV immunization has been studied in Sweden by Bottiger, who examined the persistence of IgG antibody among 250 IPV-immunized children over a period of 18 years (*35*). For the first few years, the neutralizing antibody titres fell by 0.13 to 0.22 $\log_{10}$ units per year, then levelled off to a mean decrease of 0.05 to 0.10 $\log_{10}$ units per year. At 18 years of age all the IPV-vaccinees had a neutralizing antibody titre of ≥1:16 to poliovirus types 1 and 2, and about 80% to type 3.

Duration of local immunity in the intestine

The persistence of local intestinal IgA can be analysed by studying intestinal resistance to infection with polioviruses. Sabin showed that 2 years after vaccination with type 1 OPV no intestinal poliovirus multiplication was detectable following challenge among four persons, while among three other persons there was limited multiplication (*23*). Eight persons previously immunized with type 2 OPV exhibited almost complete resistance to challenge. In contrast, among seven of the eight persons who were previously immunized with type 3 OPV, intestinal replication occurred following challenge. These data show that local intestinal immunity can persist for at least 2 years after vaccination with OPV; they also suggest that resistance following type 3 infection is low compared with that following type 1 or type 2 (*23*).

More recently Nishio et al. investigated the isolation of attenuated polioviruses from children revaccinated 10 years after the primary series of OPV (*36*). About 80% of the vaccinees had become susceptible to infection with poliovirus types 1 and 3, and 18% had become susceptible to poliovirus type 2. This susceptibility correlated with the titre of serum neutralizing antibody, i.e., susceptible individuals had lower serum antibody titres. It was suggested that a decrease in serum antibody titre could be a good indicator of reduction in intestinal local immunity and that reinfection can occur once the serum neutralizing antibody titre is ≤1:8.

Duration of local immunity in the nasopharynx

Secretory IgA antibody has been detected in the nasopharyngeal secretions of individuals 10–15 years

after natural infection with wild type 1 poliovirus (*14*). Also, studies carried out by Ogra et al. of children vaccinated with OPV showed secretory IgA antibody titres in the nasopharynx that persisted at a stable level for up to 6 years (*37*).

Boosting immunity

Effect of boosting on serum antibody

Booster doses of vaccine play an important role in prolonging the duration of humoral and local immunity. Booster immunization 8 months after the primary series of poliovirus vaccine produced a fourfold increase in IgG levels among infants vaccinated and boosted with OPV and a threefold increase in IgG levels among infants vaccinated and boosted with IPV (*38*). There was a transient reappearance of IgM antibody in both groups. The serum IgA titre exhibited a small (nonsignificant) increase in children previously vaccinated with OPV and no change in children previously vaccinated with IPV.

Effect of boosting on secretory antibody

Ogra et al. found that challenge with OPV 8 months after the primary series of OPV resulted in a very small increase in the nasopharyngeal IgA antibody levels whereas children previously vaccinated with IPV did not have any nasopharyngeal IgA antibody response (*14*). Onorato et al. found that a challenge with type 1 OPV of children previously vaccinated with OPV led to an increase in the geometric mean titre of type 1 IgA antibody in the nasopharynx and in faeces of about two $\log_{10}$ units (*17*). There was a similar increase in the titre of secretory IgA antibody among children previously vaccinated with eIPV and challenged with OPV (*17*).

Secondary boosting with OPV

In countries where OPV is used for mass vaccination, boosting can occur because of the spread of attenuated polioviruses from vaccinees to their contacts. Such spread has been demonstrated in several prospective virological and serological studies (*39, 40*). Successful spread of attenuated poliovirus from contact vaccinees depends in part on the level of sanitation in the community, but mostly on the intestinal susceptibility of the population. A study by Magrath et al. indicates that serum IgG antibody levels of about 1:32 in OPV-vaccinees prevent intestinal reinfection with a booster dose of OPV, whereas lower levels permit a boosting infection (*41*).

In countries where only IPV is used for vaccination and where no wild and no attenuated polioviruses are circulating, the duration of immunity may be shorter than in countries where OPV leads to secondary boosting. Booster doses may be needed every 10 years in countries that use only IPV (*35*). Similarly, many countries whose OPV coverage is high have included booster OPV doses, either in the routine schedule or selectively for certain age cohorts with lower levels of immunity (*42*).

Transmission of wild polioviruses

Natural infection: household studies

In the pre-vaccine era, where natural transmission of wild poliovirus occurred, about 90% of susceptible household contacts were infected, regardless of the socioeconomic and sanitary status of their families (*43*). The estimated mean duration of faecal excretion of poliovirus in an index patient was 51 days. In these household settings, poliovirus infection was also documented in previously naturally immune individuals; however, faecal excretion of poliovirus in this group was low (only 70%). This suggests that natural infection with poliovirus induces a high degree of intestinal resistance (but not 100%) to poliovirus excretion.

Prospective household studies of IPV

It has been hypothesized that widespread use of IPV could limit the spread of poliovirus because this vaccine is able to decrease pharyngeal shedding of the virus (*44, 45*). However, a large number of studies report no significant effect of IPV on intrafamilial spread of wild poliovirus (*25, 44, 46–49*). Fox et al. observed 177 episodes of household infection with poliovirus in a study group comprising more than 100 representative households (*49*). No evidence was found that primary vaccination with IPV had any influence on intestinal infection with wild poliovirus; IPV-vaccinated children appeared to be just as effective sources of intrahousehold spread of wild virus as nonvaccinated children. Another study by the same group demonstrated that mass vaccination with IPV had no influence on intrahousehold dissemination of wild polioviruses and no influence on extra-familial spread of polioviruses (*50*).

Prospective household studies of OPV

Unfortunately, there are no studies of episodes of household infection with wild polioviruses among study groups vaccinated with OPV. Because naturally immune children are ineffective sources of infection (*49*), and the intestinal tract of persons vaccinated with OPV is as resistant to poliovirus infection as that of those with naturally acquired immunity (*20*),

it is likely that the spread of poliovirus from persons vaccinated with OPV is significantly reduced compared with persons vaccinated with IPV.

Outbreaks in IPV-immunized countries

Important information about the influence of IPV and OPV on the transmission of wild poliovirus is provided by recent outbreaks of poliomyelitis.

In the Netherlands, although coverage levels for primary and booster doses of IPV have been very high for nearly 30 years, several close-knit religious groups have continued to reject immunization. The country has been nearly poliomyelitis-free for most of this period, except for intermittent appearances of wild poliovirus among the unimmunized religious groups. Small outbreaks occurred in 1961 (13 cases), 1963 (10 cases), 1966 (10 cases), and 1969 (8 cases); and larger outbreaks occurred in 1971 (39 cases), 1978 (114 cases), and in 1992–93 (71 cases) (*3, 4*). Nevertheless, subclinical infections with wild poliovirus were documented in the stools of 10–50% of IPV-immunized schoolchildren in contact with poliomyelitis cases during the 1978 type 1 outbreak (*3*). Similar findings were reported among schoolchildren during the 1992–93 type 3 outbreak (*4*).

In Sweden, IPV has been used for routine immunization since 1958. With one exception, in 1977, no indigenous cases of poliomyelitis have been identified in the country since 1962. Furthermore, no polioviruses have been isolated from about 6000 stool samples submitted each year for enterovirus testing (*51*). In 1977 a single paralytic case caused by wild type 2 poliovirus occurred involving a member of a religious group that refused immunization. Although there were no further paralytic cases, wild poliovirus was found in 40% of sewage samples from the affected community.

In Finland, IPV coverage was nearly 90% when an outbreak due to type 3 wild virus occurred in 1984–85 (*52*). Although there were only nine paralytic cases, studies showed that the wild type 3 virus was present in the stools of about 25% of IPV-immunized preschool age children. By early 1985 the Finnish epidemic type 3 strain was isolated in the sewers of Stockholm and another Swedish city close to the Finnish border (*51*). On the basis of the viruses isolated from healthy individuals and from sewage, it was estimated that at least 100 000 persons in the general Finnish population were infected (*2*). Because no wild polioviruses had circulated in Finland for a period of 20 years, no "natural" boosting of immunity (including local immunity) took place. As proposed by Hovi et al., a reduction in the proportion of persons with good mucosal immunity to type 3 poliovirus may have contributed to the spread of virus in this particular outbreak (*2*).

Outbreaks in OPV-immunized countries

Experience in the USA, where OPV has been used for many years to vaccinate against poliomyelitis, has shown that there are no longer any indigenous reservoirs of wild polioviruses in the country and that a true break in the chain of transmission of wild poliovirus has been achieved. Imported wild strains of poliovirus undoubtedly continue to be introduced, but any resulting cases of poliomyelitis are sporadic and almost never produce secondary cases (*53*). It might therefore be concluded that use of OPV induces widespread intestinal resistance to wild poliovirus, thus reducing the pool of susceptible individuals to a level below that required for perpetuation of the virus in nature; however, a number of recent outbreaks of poliomyelitis have occurred in countries with high OPV coverage, as discussed below.

In Israel, an outbreak caused by type 1 virus occurred in 1988 (*54, 55*). Most of the cases involved young adults who had been given four doses of OPV during their first year of life, but who had not received booster doses. A study carried out prior to the outbreak among under-30-year-olds found low titres of serum IgG antibody against type 1 poliovirus. Another factor in the outbreak may have been the transmission of wild poliovirus by children vaccinated with eIPV only. In one of the areas with the highest number of cases of paralytic poliomyelitis, some asymptomatic eIPV-vaccinated children were found to be excreting the wild virus.

In Oman, coverage with three doses of OPV reached 88% in 1987. But in 1988–89, a widespread outbreak of type 1 poliomyelitis occurred with 118 paralytic cases (*5*). Epidemiological studies found that the clinical efficacy of three doses of OPV was 91%. Despite this, the wide geographical distribution of the cases, the high estimated rates of infection in some regions, the unusually high titre of type 1 neutralizing antibody among control children shortly after the outbreak, and the lack of clustering of unvaccinated infants (according to an immunization record review) suggest that a substantial proportion of fully vaccinated children may have been involved in the chain of transmission of wild poliovirus (*5*).

Several other recent outbreaks have occurred in pockets of unimmunized or poorly immunized persons in countries with generally high OPV coverage, as discussed below.

In Jordan, an outbreak of type 1 poliomyelitis occurred in 1991–92. Coverage of infants with three doses of OPV had been above 90% since 1988, but coverage in the outbreak districts was only 84%. Overall, 32 cases of poliomyelitis were confirmed (*56*).

In Bulgaria, where the OPV coverage had been >95% from the mid-1980s and no cases of poliomyelitis had occurred since 1984, an outbreak due to type 1 poliovirus led to 43 paralytic cases in 1991 (*57*). More than half the cases had not been immunized, and most of them were children from gypsy families, who are sometimes reluctant to accept immunizations or were late in appearing for scheduled visits.

In Malaysia, where national immunization coverage of infants with three doses of OPV has been 90% or above since 1990, a type 1 outbreak occurred in 1992. There were three paralytic cases, all related to a religious group that refused immunization (*58*).

Unfortunately, during these recent outbreaks no comparative studies on the excretion of wild poliovirus by unvaccinated and vaccinated children were conducted. During future outbreaks, such studies would be useful to clarify the role played by the local immunity of OPV-vaccinated individuals in the transmission of wild poliovirus.

Importation of wild polioviruses

Until poliovirus has been eradicated globally, poliomyelitis-free countries will remain at risk of reintroduction of the wild virus. Faced with a wall of vaccine-induced immunity, the wild viruses will eventually perish. If they infect unimmunized individuals, however, such viruses could cause poliomyelitis. It is generally estimated that about 1 in 1000 susceptible persons who are infected with wild poliovirus will develop paralytic poliomyelitis.

In England and Wales, five cases of paralytic poliomyelitis due to imported poliovirus were reported from 1985 to 1991 (*59*). Four of the cases involved an unimmunized individual who had visited a country where poliomyelitis was endemic. The British government recommends that individuals travelling to poliomyelitis-endemic countries receive poliovirus vaccine prior to their departure (*59*).

In the USA, five cases of disease associated with imported poliovirus were reported from 1980 to 1989 (*60*). Three of these cases involved adults who had travelled to poliomyelitis-endemic countries and the remaining two involved immigrant children. The U.S. Immunization Practices Advisory Committee recommends that poliovirus vaccine be administered to travellers to endemic areas before their departure (*60*).

The risk of importation and subsequent spread of wild poliovirus to unimmunized persons was shown in 1978 when wild type 1 poliovirus from an outbreak among members of a religious group in the Netherlands led to paralytic poliomyelitis cases among other members of the same sect in Canada and the USA (*3*). This risk reappeared in 1992–93, with an outbreak of type 3 poliovirus among the same religious group in the Netherlands. In February 1993, the same wild virus was detected in stool samples from unimmunized members of the same sect in Canada, although there were no reports of paralytic illness (*61*). Epidemiological investigations revealed that there had been contact between the religious community in Netherlands and its sister community in Canada. This episode clearly documents the occurrence of wild virus importation and silent transmission.

Discussion

Breaking the chain of transmission of poliovirus is a necessary step towards achieving the goal of global poliomyelitis eradication established by the World Health Assembly in 1988. To learn how the chain of transmission can be interrupted, an understanding of the pathogenesis of poliomyelitis is useful. The following are critical factors: replication of poliovirus at the primary portal of entry (the mucosa of the oropharynx and the lower intestinal tract), entry of the virus into the bloodstream, and establishment of the infection in the central nervous system. Human immune response to poliovirus infection shows that both humoral and secretory immunity play a role in preventing the transmission of polioviruses.

Natural infection, as well as vaccination with either type of poliovirus vaccine, induces serum neutralizing antibody, which protects the individual against paralytic poliomyelitis. In at least some developing countries, however, the serum antibody response to OPV is less than optimal. For this reason, since 1984, WHO has recommended that a dose of OPV be given at birth in poliomyelitis-endemic countries (*62*). If it is not feasible to do this, countries are advised to schedule a fourth dose of OPV to be given sometime during the first year of life (e.g., at 9 months of age at the same visit as measles vaccine is administered).

To maintain high levels of protective serum antibody, booster doses of poliovirus vaccine may be considered, especially in countries where wild poliovirus is not circulating and "natural" boosting is absent. With periodic boosting, persons can remain protected against paralytic poliomyelitis for life. However, humoral immunity plays a limited role in restricting replication of poliovirus in the oropharynx or the intestine.

Over the past 35 years, many studies have shown that natural infection and successful vaccination with OPV induce local secretory immunity in

the nasopharynx and the lower intestinal tract. For 70–80% of persons who are naturally immune or who have completed a primary series of OPV, this local immunity seems to block the transmission of polioviruses. The remaining 20–30% of persons vaccinated with OPV can be expected to excrete poliovirus after infection, although for considerably shorter periods and with substantially lower poliovirus titres than those excreted by susceptible unimmunized persons.

Limited studies of susceptibility to poliovirus infection in persons vaccinated with OPV and challenged with attenuated poliovirus after several years suggest that local immunity to poliovirus is not lifelong. After 5–7 years local immunity can disappear, despite the presence of a satisfactory level of serum antibody.

Only a small proportion (20–30%) of persons immunized with IPV will develop solid intestinal immunity and will not excrete virus. Even so, those who excrete poliovirus do so for a shorter period and at a lower titre than unimmunized persons. However, this is true only if the serum neutralizing antibodies are high in the IPV vaccinee. Immunization with IPV appears to have a greater effect on virus shedding from the nasopharynx than from the intestine. Nevertheless, studies of naturally occurring poliovirus infection in IPV-vaccinated families show that vaccination with IPV has no influence on intrahousehold dissemination of wild poliovirus in any socioeconomic group. It is clear that the spread of wild polioviruses will be greater in populations immunized with IPV than in those immunized with OPV.

Recent outbreaks of poliomyelitis in countries with high levels of vaccine coverage have shown that epidemics of the disease can occur in areas that have been practically free of poliomyelitis for several years. Despite the good clinical efficacy of both IPV and OPV, a substantial proportion of fully vaccinated persons appears to be involved in the chain of transmission of wild polioviruses, especially in countries where sanitation and hygienic practices are relatively poor. Nevertheless, there is good evidence from the Region of the Americas that a break in the transmission of wild polioviruses can be achieved by intensive routine application of OPV supplemented by mass immunization techniques, including national immunization days and "mopping up" (*63*).

To decrease to the maximum extent the transmission of wild polioviruses in countries where poliovirus vaccine has been administered intensively and where no clinical cases of poliomyelitis are being registered, vaccination coverage needs to be maintained at high levels. Attention should be directed towards identifying potential pockets of low immunization coverage. Such pockets can be expected where there is geographical isolation, social isolation (gypsies, nomads, minority populations), lack of access to or of information about health services (a concern among urban slum populations and the homeless), or rejection of immunization for philosophical or religious reasons. Special efforts should be directed towards reaching the hard-to-reach with immunization services. The success of Scottish public health authorities in establishing good rapport with the gypsy community provides a good example of what can be done in this respect (*64*). Similarly, public health authorities in Bulgaria instituted special immunization sessions for gypsy children, following a poliomyelitis outbreak among them in 1991 (*57*). In the Netherlands, a coalition of religious and community leaders has initiated dialogue with communities at risk for future outbreaks.[b]

To prevent importation of wild poliovirus, the poliomyelitis vaccination status of persons travelling from poliomyelitis-free countries to endemic countries should be updated, as is now routinely recommended in several countries.

[b] **Douma J, Schaeffer JHF, Tromp T.** The non-vaccinated community. Paper presented at *WHO Meeting on Surveillance of Poliomyelitis: lessons learnt from the 1992–93 outbreak in the Netherlands, Bilthoven, 22–23 June 1993.*

Résumé

Interruption de la transmission du poliovirus sauvage par la vaccination: considérations immunologiques

En 1988, l'Assemblée mondiale de la Santé s'est fixé pour objectif l'éradication mondiale de la poliomyélite d'ici l'an 2000. Des progrès importants ont été accomplis et 43 pays n'ont signalé aucun cas associé au virus sauvage en 1993.

L'article passe en revue les considérations immunologiques concernant l'interruption de la transmission du poliovirus sauvage par la vaccination. Bien que l'immunité générale prévienne la poliomyélite au niveau individuel, c'est l'immunité locale qui importe pour empêcher la transmission du poliovirus dans la communauté. L'infection naturelle et la vaccination avec un vaccin buccal (VPO) induisent une immunité locale dans l'intestin et le nasopharynx chez environ 70 à 80% des individus. Par contre, le vaccin inactivé (VPI) ne confère une immunité locale intestinale que chez 20 à 30% des sujets. Quel que soit le vaccin utilisé, une proportion importante de la population

immunisée peut transmettre le virus sauvage. En outre, si l'immunité générale persiste longtemps, certaines données incitent à penser qu'il n'en est pas de même de l'immunité locale.

Pour interrompre la transmission du poliovirus sauvage, il importe d'atteindre et de maintenir un degré élevé de couverture vaccinale. Des flambées récentes ont montré que l'exposition au poliovirus sauvage présente un risque pour les sujets non immunisés, même lorsque la couverture vaccinale générale est élevée. La vaccination de populations difficiles à atteindre revêtira une importance croissante à mesure que les pays progresseront sur la voie de l'éradication. Les résidents des pays exempts de poliomyélite qui se rendent dans des pays où la maladie est endémique doivent s'assurer qu'ils sont correctement vaccinés.

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